Control of Nausea and Vomiting

Observations on the Use of Chlor-Trimeton® (Chlorprophenpyridamine Maleate) Syrup

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• **Chlor-Trimeton (chlorprophenpyridamine maleate) syrup was effective in preventing and controlling nausea and vomiting in 53 of 57 patients. In doses of one to four teaspoonfuls (2 to 8 mg.), it controlled nausea and vomiting following operative procedures, vomiting due to nonspecific causes, hyperemesis gravidarum, vomiting in altitude and radiation sickness, and vomiting in patients with carcinoma of the colon, acute pancreatitis, and poorly controlled diabetes.**

No untoward effects from the drug were noted.

The syrup was easy to administer, rapidly absorbed, and apparently provided a local anesthetic effect on gastric mucosa.

THE ANTIHISTAMINE Chlor-Trimeton® (chlorprophenpyridamine maleate) in syrup form rapidly relieved nausea and vomiting from various causes in 53 of 57 patients. This constitutes, so far as is known, the first report of the use of an antihistamine in this dosage form in the control of nausea and vomiting. Various other antihistamines, however, have been used orally and parenterally to prevent or relieve nausea and vomiting following surgical procedures,[4,15,25,28] hyperemesis gravidarum,[12,21] vomiting in radiation sickness,[1] psychogenic vomiting,[17] and vomiting following the administration of morphine[24] and contrast media.[2]

This clinical effect may be anticipated from some of the demonstrated actions of antihistamines. Diphenhydramine, for example, raised the threshold for electrical stimulation of the vomiting center of cats.[22] Antihistamines possess antivagal action,[11,23] as became apparent in a study of the use of Chlor-Trimeton in auricular fibrillation.[27] Such action may have been exerted by Chlor-Trimeton in reducin gastric acidity in patients with peptic ulcer, as was reported by Isaacson and co-workers[16] and by Ziporyn.[30] In a study of antihistamines in motion sickness, one investigator[5] noted that the effectiveness of these drugs "can be roughly predicted on the basis of [their] anticholinergic properties." Dimenhydrinate was reported[5,6,14] useful in motion sickness, but Chinn and co-workers[7] in a carefully controlled study concluded this drug afforded "no significant protection." Prophenpyridamine, the parent substance of Chlor-Trimeton, was one of the compounds in the group studied by Chinn that effectively protected against seasickness. The prevention and control of nausea and vomiting attendant on motion sickness by prophenpyridamine also has been shown in other studies.[8,9,10]

CHOICE OF DOSAGE FORM

Soon after a report of the control of nausea and vomiting by antihistamines intravenously,[19] a study of the oral use of Chlor-Trimeton for this purpose was begun at Santa Barbara Cottage Hospital. Chlor-Trimeton was chosen because in previous studies it had proved superior to diphenhydramine in many respects. Chlor-Trimeton syrup was used because of ease of administration, pleasant taste and rapidity of absorption. It was also thought that a syrup would spread and thus provide uniform local anesthetic action on the gastric mucosa. The similarities observed in the actions of local anesthetics, anticholinergic drugs and antihistamines[3,13,20] suggested that local anesthesia may also be a part of the action of antivomiting drugs. Local anesthetic effects have been demonstrated for antihistamines.[18,26,29] That local anesthesia was a factor in the action of Chlor-Trimeton syrup was shown in the present study by the fact that nausea was relieved almost immediately after the syrup was swallowed—too soon for the drug to be absorbed and act systemically.

PRESENT STUDY

The dosage of Chlor-Trimeton syrup for prevention or control of nausea and vomiting was determined clinically by trial and error. The dosage ultimately adopted was 4 teaspoonfuls (8 mg.) initially for nausea and vomiting and then 2 teaspoonfuls (4 mg.) every three or four hours, or as required, for nausea. No ill effects were noted from doses of

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this size nor from twice these amounts in occasional patients. No tolerance to the drug developed during administration for five to six days. In two patients who received it for two to three weeks, tolerance did develop so that even increased doses were not effective.

Postoperative nausea and vomiting. Nausea and vomiting following operation on the breast, rectum or gallbladder, appendectomy, thyroidectomy or other routine surgical procedures in 23 patients were treated with Chlor-Trimeton syrup. In 22, nausea was quickly relieved and vomiting ceased. The following brief case reports illustrate the results obtained.

CASE 1. The patient, a woman with history of severe postoperative nausea and vomiting on several occasions, had such an episode after an operation on the breast. The oral intake of fluid fell to a few cubic centimeters, which the patient could not retain. Chlor-Trimeton syrup in a dosage of 4 teaspoonfuls (8 mg.) initially and 2 teaspoonfuls (4 mg.) after three hours relieved the nausea and vomiting. After the two doses, the patient was able to take fluids orally. She was discharged the following day.

CASE 2. A man had severe nausea following ligation of a vein. He was unable to stand. Within a few minutes after the administration of Chlor-Trimeton syrup, nausea disappeared. Within an hour the patient could sit in a chair.

CASE 3. The patient, a woman, had nausea and vomiting for 24 hours after an operation on the breast. Chlor-Trimeton syrup, administered at the end of this time, relieved symptoms within five minutes. She then could readily take fluids by mouth.

Hyperemesis gravidarum. The dosage of Chlor-Trimeton syrup for the control of nausea and vomiting in pregnancy was 4 teaspoonfuls (8 mg.) on arising, with 1 teaspoonful (2 mg.) as needed for nausea. Fourteen of 15 patients were relieved by this treatment. One patient did not respond and remained refractory to all therapy for a period of two to three months. One patient developed a tolerance to the antihistamine after two to three weeks' use but by that time nausea had become minimal.

One pregnant patient with nausea and vomiting was hospitalized because of dehydration. The oral fluid intake was 300 to 400 cc. daily. This was increased to 2,100 cc. at the end of the first day after the administration of Chlor-Trimeton syrup was begun, and to 2,500 at the end of the second day. The patient was discharged without prescription for continued use of the drug. Severe nausea and vomiting recurred two days later. Another therapeutic agent used by the attending physician proved useless. Chlor-Trimeton syrup again afforded relief.

Nonspecific nausea and vomiting. All 12 patients with nausea and vomiting from nonspecific causes were satisfactorily relieved with Chlor-Trimeton syrup. One patient had vomited eight to ten times daily before receiving Chlor-Trimeton. In that case, one-half teaspoonful (1 mg.) controlled the vomiting at first. The dosage had to be increased to 1 teaspoonful (2 mg.), and then to 4 teaspoonfuls (8 mg.) because of increased tolerance. The drug was discontinued thereafter due to the large amounts necessary to control symptoms.

Other conditions. A patient with poorly controlled diabetes and extensive tuberculosis was unable to retain food and ingested fluids and had been fed intravenously for four days. The average daily oral intake of fluid was 300 cc. At the time an intravenous feeding was to have begun, Chlor-Trimeton syrup was administered instead. During the first afternoon and evening, the patient received 2 teaspoonfuls (4 mg.) of Chlor-Trimeton syrup every two hours and 2 or 3 ounces of water every 30 minutes. Severe epigastric burning was relieved almost immediately. Within a few hours, 500 cc. of water had been retained. The following day the patient retained 2,500 to 3,000 cc. of fluids and began to eat a soft diet. Two teaspoonfuls (4 mg.) of Chlor-Trimeton syrup was given for nausea. This regimen was continued for a week. The use of the antihistamine was gradually reduced and finally discontinued and the patient remained free of nausea and vomiting.

Conservative treatment and intravenous feedings for one day did not benefit one man with acute pancreatitis who had severe vomiting. Chlor-Trimeton syrup controlled the vomiting almost immediately and relieved the nausea. The patient could then take fluids and food by mouth.

Chlor-Trimeton syrup stopped vomiting in a patient with carcinoma of the colon. Nausea was satisfactorily controlled with the drug for several days preceding death from pulmonary causes.

Severe vomiting on two occasions followed x-ray therapy to the spine in one patient. On three subsequent exposures, Chlor-Trimeton syrup administered at the first sign of nausea prevented further distress.

One patient, a woman 26 years of age, who had previously become nauseated and vomited when reaching high altitudes, was treated with Chlor-Trimeton syrup and for three days while she was taking the drug the condition was controlled. Nausea and vomiting returned when the supply of syrup was exhausted.

Chlor-Trimeton syrup also was administered to two patients with nausea and vomiting following an alcoholic spree. Neither was relieved.

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